Early repolarization (ER), characterized by an elevation of the QRS-ST junction (J point) in leads other than V₁ to V₃ on the 12-lead ECG, has historically been regarded as an innocuous finding in healthy, young persons. While considered benign, the potential role of ER in arrhythmogenicity has been suggested in experimental studies. Recently, several case reports have called our attention to the association of idiopathic ventricular fibrillation (VF) to J-point elevation (with or without ST-segment elevation). In addition, recent evidence has linked ER to idiopathic VF in patients with no structural heart disease. Early repolarization (ER), characterized by an elevation of the QRS-ST junction (J point) in leads other than V₁ to V₃ on the 12-lead ECG, has historically been regarded as an innocuous finding in healthy, young persons. While considered benign, the potential role of ER in arrhythmogenicity has been suggested in experimental studies. Recently, several case reports have called our attention to the association of idiopathic ventricular fibrillation (VF) to J-point elevation (with or without ST-segment elevation). In addition, recent evidence has linked ER to idiopathic VF in patients with no structural heart disease. Early repolarization (ER), characterized by an elevation of the QRS-ST junction (J point) in leads other than V₁ to V₃ on the 12-lead ECG, has historically been regarded as an innocuous finding in healthy, young persons. While considered benign, the potential role of ER in arrhythmogenicity has been suggested in experimental studies. Recently, several case reports have called our attention to the association of idiopathic ventricular fibrillation (VF) to J-point elevation (with or without ST-segment elevation). In addition, recent evidence has linked ER to idiopathic VF in patients with no structural heart disease.

Methods

Study Population

Between April 2006 and August 2010, 964 consecutive Japanese patients with an AMI (239 women; mean age, 67±12 years) who underwent percutaneous coronary intervention in Tsukuba University Hospital, Tsukuba Medical Center Hospital, and Ibaraki Prefectural Central Hospital were retrospectively enrolled. Patients were eligible if they were 18 years or older and presented within 24 hours of the onset of the symptoms associated with an AMI. Every patient was asked for ECGs recorded well before the index event.

Key Words: ECG · myocardial infarction · ventricular fibrillation · early repolarization

Clinical Perspective on p 513

Death from VF in the setting of an acute myocardial infarction (AMI) has historically been one of the most frequent causes of sudden cardiac death. Prior investigators have evaluated the clinical and angiographic features and outcomes associated with VF in patients with an AMI. In these patients, ER might be related to the VF occurrence after the AMI. However, no studies have attempted to clarify whether or not ER is associated with VF occurrences within 48 hours after the onset of an AMI. Accordingly, the purpose of this study was to clarify this point.

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effort was taken to collect such ECGs, from which the presence of ER
was evaluated. Six hundred eighty-seven patients in whom no ECGs
recorded before the onset of the AMI were available were excluded
from this study. Furthermore, 3 patients had a type 2 (n=2) or type 3
(n=1) Brugada ECG pattern,23 and 31 had a QRS complex duration
of ≥120 ms before the onset of the AMI. Another 23 had a prior AMI.
After excluding those patients, the remaining 220 patients were fi-
nally included in this study. The mean duration from the baseline 12-
lead ECG recording to the AMI onset was 5±3 months (range, 1–12).

The primary endpoint of this study was the occurrence of sus-
tained VF within 48 hours after the onset of the AMI. The patients
were classified based on the occurrence of sustained VF within 48
hours after the onset of the AMI. The demographic and clinical data
were analyzed in both study groups. The data collection covered the
age, sex, cardiovascular risk factors, culprit artery, number of dis-
 eased coronary arteries, time from the symptom onset to arrival at
the emergency room, Killip class on admission, and infarct size (based
on a peak creatine kinase rise). Hypertension, hypercholesterolemia,
and diabetes mellitus were scored on the basis of the previous diag-
nosis and initiation of therapy. Ethical approval was obtained from
the institutional review committee of each participating hospital,
and all patients gave their written informed consent before participation.

An AMI was defined as a rise in the MB fraction of the creatine
kinase of above the 99th percentile of the upper reference limit to-
gether with symptoms of ischemia. ECG changes indicative of new
ischemia (new ST-T changes or new left bundle-branch block), and/or
development of pathological Q waves on the ECG.24 The anterior precordial
leads (V1 to V3) were excluded from the analysis of the ER to avoid
the inclusion of patients with right ventricular dysplasia or Brugada
syndrome.23,25 We also analyzed the ST-segment pattern after the J
point independently to clarify the significance of the ST-segment
characteristics according to the criteria proposed by Tikkanen26: An
upsloping ST segment was defined as an elevation of the ST segment
of ≥0.1 mV within 100 ms after the J point or a persistently elevated
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We assessed the prevalence, localization, amplitude, morphology,
and ST segment of the ER in both patient groups. Two trained in-
vestigators independently evaluated the baseline 12-lead ECGs for
the presence of ER without any knowledge of the other observer’s
judgment or the clinical information. A third observer was consulted
in the case of disagreement. All ECGs containing an ER pattern were
double-checked, and the grading was established by consensus. The
intraobserver variability was assessed in all patients. In 50 randomly
selected patients, 1 observer evaluated a new arbitrary judgment on a
separate occasion to determine the interobserver variability.

Statistical Analysis
The continuous variables are expressed as mean±SD. The compari-
sions between 2 groups were tested by an unpaired t test. We used
the log-transformed peak creatine kinase levels and time from the
symptom onset to arrival at the emergency room, as is conventionally
done. All categorical variables were presented as the number and per-
centage in each group and were compared by a χ² analysis or Fisher
exact test. An overall χ² test for a 2×n table was constructed when
comparisons involved >2 groups. A univariable of the patient charac-
teristics was compared between the VF occurrence group and no VF
occurrence group, and a logistic regression analysis was performed to
detect any independent significant predictors by adjusting with multi-
variables (reported as odds ratios [OR] with 95% confidence intervals
[CIs]). The intraobserver and interobserver variability was investi-
gated by κ statistics. All analyses were performed using the PASW
17.0 software package (SPSS, Chicago, IL). P<0.05 was considered
statistically significant.

Results
Demographic and Clinical Characteristics of All AMI Patients
Among the 220 patients in whom the 12-lead ECGs before the
AMI onset were obtained, 21 (10%) patients had an

Figure 1. Baseline ECGs from patients
with early repolarization. This shows 2
patients with a J-point elevation of ≥0.2
mV. A, Notched elevation (arrows) in
the inferior leads; B, slurred elevation
(arrows) in the inferior and lateral leads.

ECG Analysis
To blind the ECG interpreters from the clinical characteristics and
patient grouping, all tracings were scanned and coded. The early re-
polarization patterns were stratified according to the degree of the
J-point elevation (≥0.1 mV) that was either slurred (a smooth transi-
tion from the QRS segment to the ST segment) or notched (a positive
J-deflection inscribed on the S wave) in at least 2 consecutive inferior
leads (II, III, and aVF), lateral leads (I, aVL, and V4 to V6), or both
(Figure 1).12,20 The J-point amplitude was measured at the QRS-ST
junction in case of slurred J waves or the peak J point in the case of
notched J waves, and relative to the QRS onset to minimize any base-
line wandering effect.16 We analyzed the inferior and lateral J-point
elevation independently to clarify the significance of the localization
and used 2 predefined cutoff points (≥0.1 mV and ≥0.2 mV) to as-
sess the significance of the amplitude of the J-point elevation from
baseline. The morphological characteristics of the ER (notching or
slurring) were also analyzed independently.6,13 The anterior precordial
leads (V1 to V3) were excluded from the analysis of the ER to avoid
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episode of VF within 48 hours after the onset of the AMI, and the remaining 199 (90%) did not. VF occurred before catheterization in 13 patients, during catheterization in 7, and after catheterization but within 48 hours after the onset of the AMI in the remaining patient. There was no significant difference in the age or prevalence of cardiovascular risk factors between these 2 groups (Table 1). However, the patients with VF had a greater prevalence of a male sex \((P<0.05)\) and shorter duration from the symptom onset to the arrival at the emergency room \((P<0.001)\) than those without (Table 1). Although the culprit artery, peak creatine kinase level, or prevalence of an STEMI did not differ between the 2 groups, the patients with VF had a greater number of diseased coronary arteries \((P<0.05)\) and Killip class on admission \((P<0.001)\) than those without (Table 1). Furthermore, with the analysis of the 12-lead ECG recorded before the AMI, ER was found in 10 (48%) of the patients with VF, which was more prevalent than in those without \((12\%; P<0.001; \text{Table 1})\).

**Predictors of VF Occurrence During an AMI**

A multivariate logistic regression analysis revealed that a time from the symptom onset to the arrival at the emergency room of \(<180\) minutes \((OR, 3.77; 95\% \text{ CI}, 1.13–12.59; P<0.05)\), Killip class greater than I \((OR, 13.60; 95\% \text{ CI}, 3.43–53.99; P<0.001)\), and the presence of ER \((OR, 7.31; 95\% \text{ CI}, 2.21–24.14; P<0.01)\) were associated with the occurrence of VF within 48 hours after the onset of the AMI (Table 2). Male sex, the peak creatine kinase level, and the presence of ST-segment elevation or multivessel disease were

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**Figure 2.** Representative case of preserved early repolarization. **A,** Baseline 12-lead ECG obtained 6 months before the acute myocardial infarction (AMI) onset shows a notched early repolarization with an upsloping ST segment in the inferior leads. **B,** Twelve-lead ECG during the onset of an anterior AMI showing preserved early repolarization in the inferior leads.

**Figure 3.** Representative case with serial 12-lead ECGs who consecutively had anterior and inferior acute myocardial infarction (AMI) within 3 months of each other. **A,** Baseline 12-lead ECG obtained 1 month before the AMI onset demonstrating a notched early repolarization (ER) with a horizontal/descending ST segment in the inferior leads (horizontal ST segment in leads II and aVF; descending ST segment in lead III). **B,** ECG obtained at the onset of an anterior AMI showing the lack of ER because of reciprocal ST-T changes in the inferior leads. **C,** At 2 weeks after the onset of the anterior AMI, the J point was reelevated in the inferior leads. **D,** Three months after an anterior AMI onset, the case had an inferior AMI, and the ECG at that time demonstrated no ER. **E,** The ER had still vanished 2 weeks after the inferior AMI onset.
Early repolarization in the inferior leads was associated with an increased occurrence of VF before the statistical adjustment (38% versus 9%; \( P < 0.01 \); Table 1) and after adjusting for multivariables (OR, 6.85; 95% CI, 2.01–23.39; \( P < 0.01 \); Table 3).

**Magnitude and Morphology**
A J-point elevation of \( >0.2 \) mV was found in the inferior or lateral leads in 17 (8%) subjects, and the presence of a J-point elevation of \( >0.2 \) mV in the inferior or lateral leads was associated with an increased occurrence of VF (29% versus 6%; \( P < 0.01 \); Table 1). A multivariate logistic regression analysis demonstrated that a J-point elevation of \( \geq 0.2 \) mV in the inferior leads was an independent predictor of the occurrence of VF before the statistical adjustment (38% versus 9%; \( P < 0.01 \); Table 1) and after adjusting for multivariables (OR, 6.85; 95% CI, 2.01–23.39; \( P < 0.01 \); Table 3).
occurrence of VF (OR, 10.65; 95% CI, 2.35–48.34; \( P < 0.01 \); Table 3).

The prevalence of a notched early repolarization significantly differed between the patients with VF and those without (38% versus 9%; \( P < 0.01 \); Table 1). In contrast, the incidence of slurring did not differ between the 2 groups (\( P = 0.2 \); Table 1). A multivariate logistic regression analysis revealed that a notched early repolarization in the inferior leads was associated with the occurrence of VF (OR, 4.88; 95% CI, 1.36–17.57; \( P < 0.05 \); Table 3).

### ST Segment

The prevalence of early repolarization with a horizontal/descending ST segment significantly differed between the patients with VF and those without VF (43% versus 8%; \( P < 0.001 \); Table 1). Conversely, the incidence of an upsloping ST segment did not differ between these 2 groups (\( P = 0.6 \); Table 1). A multivariate logistic regression analysis demonstrated that a J-point elevation in the inferior leads with a horizontal/descending ST segment was an independent predictor of the occurrence of VF (OR, 8.05; 95% CI, 2.18–29.70; \( P < 0.01 \); Table 3).

### Changes in the Early Repolarization Pattern Before and Just After the Onset of the AMI

Among the 34 patients who had ER in the baseline 12-lead ECG recording before the AMI, ER was still observed in the 12-lead ECG, which was recorded on admission due to the onset of an AMI in 19 (56%) patients (Figure 2). However, in the remaining 15 (44%) patients, it was not definitely confirmed on admission for an AMI (Figure 3). Conversely, among the 186 patients who had no ER in the baseline 12-lead ECG before the AMI, no patients developed any ER in the 12-lead ECG on admission.

### Reproducibility of the Judgment of Early Repolarization

The intraobserver variability of the ER was \( \kappa = 0.93 \) (\( P < 0.001 \)) and interobserver variability, \( \kappa = 0.87 \) (\( P < 0.001 \)).

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### Table 2. Univariate and Multivariate Logistic Regression Analyses of Ventricular Fibrillation Occurrence

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariate</th>
<th>Multivariate*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds Ratio (95% CI)</td>
<td>( P ) Value</td>
</tr>
<tr>
<td>Age per year</td>
<td>0.983 (0.945–1.022)</td>
<td>0.381</td>
</tr>
<tr>
<td>Male sex</td>
<td>7.832 (1.027–59.754)</td>
<td>0.047</td>
</tr>
<tr>
<td>Time from the symptom onset to ER of &lt;180 minutes</td>
<td>2.468 (0.978–6.227)</td>
<td>0.056</td>
</tr>
<tr>
<td>A Killip class greater than I</td>
<td>7.653 (2.815–20.807)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peak creatine kinase levels &gt;3000 U/L</td>
<td>2.495 (0.989–6.291)</td>
<td>0.053</td>
</tr>
<tr>
<td>No. of diseased coronary arteries &gt;1</td>
<td>2.629 (0.980–7.052)</td>
<td>0.055</td>
</tr>
<tr>
<td>ST-elevated myocardial infarction</td>
<td>5.677 (0.741–43.492)</td>
<td>0.095</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.448 (0.508–4.130)</td>
<td>0.489</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.295 (0.521–3.219)</td>
<td>0.579</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.374 (0.554–3.406)</td>
<td>0.493</td>
</tr>
<tr>
<td>Early repolarization</td>
<td>6.629 (2.546–17.256)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

ER indicates emergency room.

*All the variables in the columns were used in the multivariate model.

### Table 3. Univariate and Multivariate Logistic Regression Analyses of Ventricular Fibrillation, According to the J-Point Pattern in the Inferior Leads*

<table>
<thead>
<tr>
<th>Variables</th>
<th>VF, n (%)</th>
<th>Univariate</th>
<th>Multivariate*</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Odds Ratio (95% CI)</td>
<td>( P ) Value</td>
</tr>
<tr>
<td>No J-point elevation (n=186)</td>
<td>11 (6)</td>
<td>1.000</td>
<td></td>
</tr>
<tr>
<td>J-point elevation of ≥0.1 mV in the inferior leads (n=26)</td>
<td>8 (31)</td>
<td>6.188 (2.265–16.906)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>J-point elevation of ≥0.2 mV in the inferior leads (n=14)</td>
<td>6 (43)</td>
<td>9.550 (2.929–31.135)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>J-point notched elevation of ≥0.1 mV in the inferior leads (n=22)</td>
<td>7 (32)</td>
<td>6.133 (2.149–17.507)</td>
<td>0.001</td>
</tr>
<tr>
<td>Inferior J-point elevation with a horizontal/descending ST segment (n=21)</td>
<td>8 (38)</td>
<td>8.805 (3.097–25.033)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

VF indicates ventricular fibrillation.

*The variables that were included in the multivariate analyses were the age, sex, time from symptom onset to arrival in the emergency room of <180 minutes, Killip class of greater than I, peak creatine kinase levels >3000 U/L, number of diseased coronary arteries >1, ST-elevated myocardial infarction, hypertension, diabetes mellitus, and smoking.
Discussion

Major Findings
The results of this study demonstrated for the first time the following findings: (1) approximately 15% of the AMI patients had ER in the 12-lead ECG before the AMI onset; (2) about 50% of the patients who had VF within 48 hours after the AMI onset had ER, and the presence of ER was an independent predictor for a VF occurrence within 48 hours after the AMI onset after an adjustment for multivariables; (3) as features of the ER pattern, a J-point elevation in the inferior leads, greater magnitude of the J-point elevation, notched morphology of the ER, and ER with a horizontal/descending ST segment, all were significantly associated with the occurrence of VF; (4) the ER pattern disappeared or was not well recognized in the 12-lead ECG shortly after the AMI onset in 44% of the patients who had ER; and (5) none of the patients without any ER before the AMI onset had any ER after the AMI.

Proposed Mechanism of VF in AMI Patients Who Have Early Repolarization
In the present study, in addition to an early presentation and a Killip class of greater than I, which have been reported as risk factors for VF during the early phase of an AMI,18–22 we found for the first time that the presence of ER was a new risk factor for a VF occurrence even after an adjustment for multivariables.

Transmural differences in the early phases (phases 1 and 2) of the cardiac action potential, which are created by a disproportionate amplification of the repolarizing current in the epicardial myocardium due to a decrease in the inward sodium or calcium channel currents or an increase in the outward potassium currents mediated by the I_n, I_A, and I_KCa channels, are considered to be responsible for the inscription of the ECG J wave.26 The trigger and substrate for the development of phase 2 reentry and ventricular tachycardia/VF may eventually emerge from the transmural dispersion of the duration of the cardiac action potentials.26

Clinical observations suggest an association between the I_n density and risk of primary VF during an AMI.26 The presence of a more prominent I_n in males than in females, which is thought to be causative for the predominance of ER in men,27 may account for the 1.3 fold higher prevalence of sudden cardiac death in males than in females.20 A much greater predominance of the I_n in the right ventricular epicardium than in the left ventricular epicardium29 might also explain a higher prevalence of primary VF in patients with an acute inferior MI who have right ventricular involvement than in those without or in those with an anterior MI.29

The loss of the right ventricular epicardial action potential dome in the ischemic region can lead to a closely coupled extrasystole through phase 2 reentry.30,31 Thus, the fundamental mechanisms responsible for the ST-segment elevation and initiation of VF in the early phases of an AMI are considered to be similar to those in the inherited J-wave syndromes.26,30,31 When an AMI occurs in patients who have ER, the mechanisms described above might appear more strongly than in those who do not have ER, and it might cause VF.

Characteristics of the Pattern of Early Repolarization in AMI Patients With VF
Previous studies have demonstrated the characteristics of ER in those who have had VF; a J wave was found in the inferior leads in many patients with idiopathic VF9,11,13; the J waves were indeed taller in the idiopathic VF group10,13,15; the presence of “slurring” was not useful for identifying patients with idiopathic VF9,13 and tachyarrhythmias due to chronic coronary disease16; and patients with ER and a horizontal/descending ST variant had an increased hazard ratio of arrhythmic death.12–14

In the present study, the distribution, amplitude, morphology, and ST-segment characteristics of the ER in the patients with VF in the early phase of an AMI were quite similar to those of the previous findings.8–16 We think that the patients who have had those characteristic ER patterns are more susceptible to VF occurrence than those who have not.

Clinical Implications
Our study demonstrated that ER was an independent predictor of a VF occurrence in AMI patients and that those patients have a risk of a VF occurrence during an AMI that is 6 times greater than that in those without ER. In particular, much attention should be paid to the patients with ER in the inferior leads, a greater magnitude of the J-point elevation, a notched morphology of the ER, and an ER with a horizontal/descending ST segment in the early phase of an AMI. In those patients with ER, primary prevention of an AMI is more important than in those without.

Because of the ECG changes caused by the AMI itself, there is a high possibility that a preexisting ER might be missed with the evaluation of the ECG recorded during or shortly after the AMI onset. Therefore, the presence or absence should be assessed in an ECG that is recorded before the AMI onset. If there is no ECG available before the AMI onset on hand, a previously recorded ECG should be collected whenever possible to clarify the risk for VF.

Study Limitations
First, the approximately 10% prevalence of VF in this study appeared to be higher than that of the previous studies.18,20,22 The prevalence of ER before the onset of an AMI was 15%, which was comparable to that in a previous study from Japan.32 However, it was also higher than that of the previous studies in the general population of Western countries.11 The age, sex, and race-ethnic differences between this study and the previous studies might account for the differences in the prevalence of both VF and ER.11,18,20,22 A recent study with Japanese patients demonstrated that the incidence of in-hospital ventricular tachycardia/VF during an AMI was 13.3%,33 which was also higher than that of the previous studies conducted in Europe and the United States.18,20,22 Another plausible reason might be due to the adequate management of VF before catheterization. The recent spread of the use of automated external defibrillators outside the hospital and bystander cardiopulmonary resuscitation in Japan may decrease the
sudden cardiac death but increase the prevalence of VF episodes before catheterization during the acute phase of an AMI. In this study, among 13 patients who had VF episodes before catheterization, 5 patients received an appropriate shock using automated external defibrillators before arrival at the hospital, which might contribute to the high prevalence of VF in this study. Second, the small sample size limits our power and is reflected in the broad confidence intervals, most notably in the adjusted statistical analyses regarding the incidence of ER. Third, because the presence of ER was assessed with only one 12-lead ECG obtained before the AMI onset, we could not evaluate the time course and reproducibility of the ER, and the prevalence of the ER might have been underestimated.4,8,10 Fourth, the information on hypokalemia, a lack of pretreatment angina, chronic kidney disease, and a family history of sudden cardiac death, which have been reported as independent predictors of VF occurrence in patients with an AMI,19–22 were lacking in this study. Therefore, further prospective studies with a larger sample size, long-term follow-up, and the participation of many hospitals may be needed to resolve these limitations and to ensure and enhance our results.

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Disclosures

None.

References

CLINICAL PERSPECTIVE

Previous studies have reported that early repolarization (ER) was associated with idiopathic ventricular fibrillation (VF). The purpose of this study was to clarify whether or not the presence of ER in the ECG recorded before an acute myocardial infarction (AMI) onset is associated with VF occurrences in the very early phase of an AMI. In the present study, in addition to an early presentation and Killip class of greater than I, which have been reported as risk factors for VF during the early phase of an AMI, we demonstrated for the first time that the presence of ER was a new risk factor for a VF occurrence even after an adjustment for multivariables. As features of an ER pattern, a J-point elevation in the inferior leads, greater magnitude of the J-point elevation, notched morphology of the ER, and ER with a horizontal/descending ST segment, all were significantly associated with the occurrence of VF; therefore, we might recognize these patterns of ER as “malignant ER.” In patients with ER, primary prevention of an AMI is more important than in those without. The ER pattern disappeared or was not well recognized in the ECG shortly after an AMI onset in 44% of the patients who had ER in the ECG recorded before an AMI onset; therefore, the presence or absence should be assessed in an ECG that was recorded before the onset of an AMI. Further prospective validation is necessary to confirm and enhance these findings.
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